

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
29 September 2005 (29.09.2005)

PCT

(10) International Publication Number  
**WO 2005/089765 A1**

(51) International Patent Classification<sup>7</sup>: **A61K 31/51**

(21) International Application Number:  
PCT/US2005/008439

(22) International Filing Date: 15 March 2005 (15.03.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/553,168 15 March 2004 (15.03.2004) US

(71) Applicant and

(72) Inventor: HOWARD, James, R. [US/US]; P.O. Box 191,  
Brawley, California 92227 (US).

(74) Agents: JOHNSON, Barbara, E. et al.; 700 Koppers  
Building, 436 Seventh Avenue, Pittsburgh, Pennsylvania  
15219-1818 (US).

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, GR, GU, HD, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ,  
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,  
ZM, ZW.

(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,  
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: ENZYME COFACTOR COMBINATION FOR SUPPLEMENTING PYRUVATE DEHYDROGENASE AND ALPHA  
KETOGLUTERATE DEHYDROGENASE COMPLEXES

(57) Abstract: The present invention provides a method and pharmaceutical composition for preventing or treating the development of syndromes related to dysfunctional energy metabolism, such as neuropathy, spontaneous nocturnal muscle cramps associated with neuropathy, seizing, diabetes mellitus; pediatric hypoglycemia; myopathy; muscle fatigue; muscle spasms; somnolence; reduced mental acuity; exercise intolerance and myocardial insufficiency, which are due to cofactor deficiencies associated with the pyruvate dehydrogenase complex and the alpha-ketoglutarate dehydrogenase (a-ketoglutarate dehydrogenase) complex in humans or other mammals in need thereof. In particular, a method of preventing or treating at least one syndrome related to defective glucose metabolism in humans or other mammals is provided comprised of administering a combination of enzyme cofactors containing therapeutically effective amounts of thioctic acid, niacinamide, pantothenate, riboflavin and thiamine. Also provided is a pharmaceutical composition comprised of a carrier and the combination of cofactors.

WO 2005/089765 A1